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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,786	04/11/2001	David J. Diller	1073.060A	4635

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EXAMINER
LY, CHEYNE D

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

		Application No.	Applicant(s)
Office Action Summary		09/832,786	DILLER ET AL.
		Examiner	Art Unit
		Cheyne D Ly	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _25 October 2004_.

2a)☐ This action is **FINAL**.   2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1-15_ is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _1-15_ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All   b)☐ Some * c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
    Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413)
    Paper No(s)/Mail Date. _____ .

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments filed October 25, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Claims 1-15 are examined on the merits.

3. NON-FINAL OFFICE ACTION.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 6-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 6-10 are vague and indefinite because the steps in the body of the claim recite the limitation of "means for..." which has been reasonably construed as the attempt by Applicant to invoke 35 U.S.C. 112, sixth paragraph. However, the metes and bounds of the claim have not been specifically defined for the limitation of "means for..." in the specification. It is noted that Applicant discloses "computer readable program code means for providing and facilitating the capabilities of the present invention" (pages 39-40, [0097]), wherein the

specification is not clear as to whether a computer system(s) is required to implement each of

the means-plus-function step in claims 6-10 as embodied in the computer usable media. The

instant disclosure does not defined the structures necessary for each "means for 35 U.S.C.

112, sixth paragraph states that a claim limitation expressed in means-plus-function language

"shall be construed to cover the corresponding structure...described in the specification and

equivalents thereof." "If one employs means plus function language in a claim, one must set

forth in the specification an adequate disclosure showing what is meant by that language. If

an applicant fails to set forth an adequate disclosure, the applicant has in effect failed to

particularly point out and distinctly claim the invention as required by the second paragraph

of section 112." In re Donaldson Co., 16 F.3d 1189, 1195, 29 USPQ2d 1845, 1850 (Fed. Cir.

1994) (in banc). (See MPEP 2181 [R-2]).

CLAIM REJECTIONS - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in
> section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are
> such that the subject matter as a whole would have been obvious at the time the invention was made to a person
> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the
> manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the

claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent

any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to

point out the inventor and invention dates of each claim that was not commonly owned at the

time a later invention was made in order for the examiner to consider the applicability of 35

U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-3, 5-8, 10-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable

over Ho et al. (1994) taken with Rarey et al. (J. Mol. Biol., 1996).

RESPONSE TO ARGUMENT

10. Applicant's argument directed to Rarey et al. (J. of Computer Aided Molecular Design),

on page 8, 3rd paragraph, has been found to be persuasive. Therefore, the previously applied

35 U.S.C. 103(a) rejections, mailed June 25, 2004, has been withdrawn.

11. Ho et al. (1994) taken with Rarey et al. (J. Mol. Biol., 1996) describes the argued

limitations as recited in claims 1-3, 5-8, 10-13, and 15.

12. Specific to the argument that claims 1, 6, and 11 are directed to rating the

complementarity of an entire combinatorial library, Ho et al. describes the various compound

databases have inherent strengths and weaknesses (assessing) with regard to particular

chemical classes (clustering). Further, an initial database of fragments is necessary, ligand

diversity is assured through the combinatorial assortment of building blocks (page 214,

column 1, lines 11-15, and lines 33-37).

13. Specific to the argument that "Rarey is directed to docking a single molecular fragment",

Rarey et al. describes a method for screening larger sets of ligands for their binding affinity

to a given receptor (page 472, column 1, lines 21-23).   Rarey et al. describes via the images

in Figures 8 and 9, for each protein-ligand interaction, a pair of matching points (hot spots) is generated resulted from searching for new interactions (page 476, column 2, Searching for new interactions section).

14. The citation of the prior art below provides a prima facie case of obviousness as directed to the claimed invention.

BASIS FOR REJECTION

15. Ho et al. describes the various compound databases have inherent strengths and weaknesses (assessing) with regard to particular chemical classes (clustering). Further, an initial database of fragments is necessary, ligand diversity is assured through the combinatorial assortment of building blocks (page 214, column 1, lines 11-15, and lines 33-37), as in instant claim 1, lines 1-4. Ho et al. describes the "common core" as defined in the instant specification, page 5, paragraph 21.

16. "Fragments must be screened and edited to ensure steric and electrostatic complementarity...To accomplish this, all structures would have to be considered in regard to all bond loci in space as well as the structures and phramacophoric elements associated with them" (page 214, column 1, lines 43-46). By setting this constant distance to the radius of a molecular atom type, steric contacts are revealed where penetration of the receptor molecular surface by the ligand vector model occurs (page 214, column 2, last line, to page 215, column 1, line 4). In the generation of fragments for the chain_dbase database the

structures were docked in the active site with the appropriate orientation (page 216, column 1, last paragraph), as in instant claim 1, lines 5-8.

17. However, Ho et al. does not describe the limitation of determining the RMS deviation, forming clusters, and rating based on the clusters formed.

18. Rarey et al. describes a method for screening larger sets of ligands for their binding affinity to a given receptor (page 472, column 1, lines 21-23). The ligand is divided into fragments. The base placement algorithm finds positions of the base fragment in the active site (page 474, column 1, lines 18-31). The second step in the base placement algorithm is to cluster the placements according to an appropriate distance function such as rms deviation between two placements (page 475, column 1, lines 33-37). Rarey et al. uses a hierarchical clustering algorithm as applied to rms deviations (page 46, column 2, The hierarchical clustering algorithm section). A binding mode closely approaching the experimental geometry is predicted among the few highest-ranking placements (page 472, column 1, lines 23-26), as in instant claim 1, lines 9-15, and claim 2.

19. Rarey et al. further, describe the use of a cubic grid covering three-dimensional space aligned to the Cartesian coordinate axis. The grid is for checking a ligand atom for overlap with the receptor by inspecting the receptor atoms whose centers (center of mass) are located in all cubes intersecting a sphere centered in the ligand atom (page 476, column 1, line 57, to column 2, line 10). The distance between placements is the rms deviation between the

coordinates of the ligand (rms threshold 0.7A) (page 477, column 2, lines 39-45), as in

instant claim 3.

20. Rarey et al. describes via the images in Figures 8 and 9, for each protein-ligand

interaction, a pair of matching points (hot spots) is generated resulted from searching for new

interactions (page 476, column 2, Searching for new interactions section). Further, Rarey et

al. describes the docking procedure comprising FLEXX analyzing the structure of the ligand

and detects local topological symmetries at single bonds whose torsion angle can be changed

(vary). The computation of rms deviations also considers this local symmetry (page 478,

column 1, The ligand section). While, the receptor has with defined coordinates and

crystalline position (fixed) (478, column 1, The receptor section), as in instant claim 5.

21. Ho et al. implements software program in an SGI-380 (page 217, column 1, lines 35-38)

for the described method. Rarey et al. implements the FLEXX docking tool on a SUN

SPARC station 20 (page 486, column 1, Summary of results), as in instant claims 6-8, 10-13,

and 15.

22. Ho et al. describes the improvement to meet the needs necessary for understanding

receptor ligand binding for novel drug development (page 213, column 1, Introduction

section). Rarey et al. describes the increasing interest in automatic screening of ligand

databases by computational methods in the in the drug discovery process (page 470,

Introduction section, columns 1-2). Therefore, one of ordinary skill in the art at the time of

the instant would have been motivated by Ho et al. to develop improvements directed to

understanding receptor ligand binding for novel drug development as taught by Rarey et al.

Therefore, it would have been obvious to one of skill in the art at the time of the invention

was made to use the method, system and program for assessing a combinatorial library as

taught by Ho et al. and Rarey et al.

23. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ho et al.

(1994) taken with Rarey et al. (J. Mol. Biol., 1996) in view of Aldenderfer et al. (1984).

24. Ho et al. discloses a method and a system to search for complementary components in a

chemical library and Rarey et al. discloses a method for ranking ligands based on rms

deviations as cited above, as in instant claims 1-3, 5-8, 10-13, and 15. Further, Rarey et al.

describes the advantages and disadvantages to using hierarchical clustering algorithm as

applied to rms deviations (page 46, column 2, The hierarchical clustering algorithm section).

25. However, Ho et al. and Rarey et al. do not disclose the limitations of forming clusters

using a single linkage-clustering algorithm.

26. Aldenderfer et al. discloses a review of hierarchical clustering methods including single-

linkage clustering algorithm (page 39-40), as in claims 4, 9, and 14.

27. Ho et al. describes the improvement to meet the needs necessary for understanding receptor ligand binding for novel drug development (page 213, column 1, Introduction section). Rarey et al. describes the increasing interest in automatic screening of ligand databases by computational methods in the in the drug discovery process requiring a hierarchical clustering algorithm (page 470, Introduction section, columns 1-2). Therefore, one of ordinary skill in the art at the time of the instant would have been motivated by Ho et al. to develop improvements directed to understanding receptor ligand binding for novel drug development requiring a hierarchical clustering algorithm as taught by Rarey et al. and Aldenderfer et al. Therefore, it would have been obvious to one of skill in the art at the time of the invention was made to use the method, system and program for assessing a combinatorial library with a single linkage clustering algorithm as taught by Ho et al., Rarey et al., and Aldenderfer et al.

28. It is noted that cited references are not provided with the instant Office Action because they are either previously cited or considered in the IDS, filed September 26, 2003.

CONCLUSION

29. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. The USPTO's official fax number is (571) 273-8300.

30. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the

USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives

are available to answer your questions daily from 6 am to midnight (EST). The toll free

number is (866) 217-9197. When calling please have your application serial or patent

number, the type of document you are having an image problem with, the number of pages

and the specific nature of the problem. The Patent Electronic Business Center will notify

applicants of the resolution of the problem within 5-7 business days. Applicants can also

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The USPTO's PAIR system provides Internet-based access to patent application status and

history information. It also enables applicants to view the scanned images of their own

application file folder(s) as well as general patent information available to the public.

31. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-

9199.

32. Any inquiry concerning this communication or earlier communications from the

examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The

examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

C. Dune Ly
4/4/05